Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Prevention and treatment of rash in patients treated with EGFR inhibitor therapies.

Bibliographic Source(s)

Alberta Provincial Thoracic Malignancies Team, Alberta Provincial Gastrointestinal Tumour Team, Alberta Provincial Head and Neck Tumour Team. Prevention and treatment of rash in patients treated with EGFR inhibitor therapies. Edmonton (Alberta): CancerControl Alberta; 2012 May. 15 p. (Clinical practice guideline; no. SUPP-003). [73 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Recommendations for Prevention/Prophylactic Treatment of Rash

1. Epidermal growth factor receptor (EGFR) inhibitors should be administered at their maximum tolerable doses for obtaining the most effective outcomes, and should be accompanied with appropriate supportive care or preventive measures to counteract the rash.
2. Patients treated with EGFR inhibitors should receive detailed information and counseling regarding the occurrence, timing and severity of expected toxicities. Front-line caregivers of these patients should also be aware of appropriate management strategies and patient information needs, with the goal of minimizing toxicity, maximizing compliance with therapy, and maintaining a good health-related quality of life.

Recommendations for Clinical Management of Rash

3. The overall management strategy should be individualized, depending on the type, severity, and extent of toxicity caused by the therapy, and should involve a multidisciplinary team of healthcare providers.
4. Patients with mild-to-moderate rash should be treated with topical 2% clindamycin plus 1% hydrocortisone lotion twice daily until resolution of the rash.
5. Patients with moderate-to-severe rash should be treated with topical 2% clindamycin plus 1% hydrocortisone lotion twice daily until resolution of the rash, plus oral minocycline 100 mg twice daily for a minimum of 4 weeks and continuing until resolution of the rash.
6. Patients with persistent rash should be considered for a dose reduction of EGFR inhibitor therapy, as per label, and be treated with topical 2% clindamycin plus 1% hydrocortisone lotion twice daily until resolution of the rash, plus oral minocycline 100 mg twice daily for a minimum of 4 weeks and continuing until resolution of the rash, plus Medrol dose pack.

Recommendations for Supportive and Follow-up Care

7. The following supportive care measures may prevent or minimize the severity of rash associated with EGFR inhibitor therapy:
    - Use of cool or lukewarm (not hot) water for bathing or washing, and application of moisturizers immediately after bathing (to prevent skin drying)
    - Use of alcohol-, fragrance-, and dye-free soaps, shampoos, and body washes
    - Use of alcohol-free emollient creams
    - Use of hypoallergenic makeup
    - Avoidance of any skin care products containing alcohol
    - Avoidance of over-the-counter acne medications (e.g., benzoyl peroxide)
    - Avoidance of scented laundry detergents
    - Avoidance of sun exposure, and daily use of sunscreen with an sun protection factor (SPF) of 30 or higher when exposed to the sun
    - Remain well-hydrated at all times

Clinical Algorithm(s)

An algorithm titled "Treatment Pathway for the Management of EGFRI-induced Rash" is provided in the original guideline document.

Scope

Disease/Condition(s)

- Cancer (advanced non-small cell lung cancer, colorectal cancer, head/neck cancer, breast cancer)
- Epidermal growth factor receptor (EGFR) inhibitor associated rash

Guideline Category

Prevention

Treatment

Clinical Specialty

Dermatology

Oncology

Radiation Oncology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To provide recommendations for the prevention and treatment of epidermal growth factor receptor (EGFR) inhibitor associated rash that are

based on the available published evidence, combined with expert opinion and current clinical practice in Alberta

Target Population

Adult patients with advanced non-small cell lung cancer, colorectal cancer, head/neck cancer, or breast cancer treated with the epidermal growth factor receptor inhibitors cetuximab, erlotinib, gefitinib, panitumumab, or lapatinib, either alone or in combination with other treatments

Interventions and Practices Considered

1. Providing detailed information and counseling to patients who are treated with epidermal growth factor receptor (EGFR) inhibitors about expected toxicities
2. Individual therapy for rash management based on type, severity, and extent of toxicity
    - Topical 2% clindamycin plus 1% hydrocortisone lotion
    - Oral minocycline
    - Medrol dose pack
    - Dose reduction of EGFR inhibitor therapy
3. Supportive and follow-up care

Major Outcomes Considered

- Incidence of rash associated with epidermal growth factor receptor (EGFR) inhibitor therapies
- Timing of rash presentation
- Association between rash and response to anti-EGFR therapy
- Accuracy of rash grading scales
- Effectiveness of prophylactic interventions
- Effectiveness of treatment for rash resolution
- Health-related quality of life

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Research Questions

Specific research questions to be addressed by the guideline document were formulated by the guideline lead(s) and Knowledge Management (KM) Specialist using the PICO question format (patient or population, intervention, comparisons, outcomes).

Guideline Questions

- What are the signs and symptoms of rash associated with epidermal growth factor receptor (EGFR) inhibitor therapy in adult patients?
- What is the evidence for the relationship between rash and response to treatment in adult patients with advanced non-small cell lung cancer, colorectal cancer, head and neck cancers, or breast cancer treated with EGFR inhibitors?
- What are the recommended strategies for the prevention of rash associated with EGFR inhibitor therapy in adult patients with advanced non-small cell lung cancer, colorectal cancer, head and neck, or breast cancers?

- What are the recommended strategies for clinical management of rash associated with EGFR inhibitor therapy in adult patients with advanced non-small cell lung cancer, colorectal cancer, head and neck, or breast cancers?

Search Strategy

An environmental scan of the literature was first performed, in order to become familiar with the topic and to identify relevant search terms. A structured literature search was conducted using the MEDLINE/PubMed (1948 to January Week 1, 2012), EMBASE (1996 to 2012 Week 01), Cochrane Database of Systematic Reviews (2005 to December 2011), Cochrane Central Registry of Controlled Trials (1st Quarter 2012), CINAHL Plus with Full Text (2000 to present), and the International Pharmaceutical Abstracts Database (1970 to December 2011) electronic databases. The MeSH headings and search terms used in MEDLINE were: Skin, Skin Diseases, Exanthema, Drug Eruptions (Chemically Induced, Drug Therapy, Prevention & Control), Acneiform Eruptions (Chemically Induced, Drug Therapy, Prevention & Control), erlotinib, gefitinib, cetuximab, panitumumab, and Receptor, Epidermal Growth Factor (Antagonists & Inhibitors, Drug Effects). The search strategy were modified and repeated for each of the other electronic databases.

Articles were excluded from the final review if: they addressed skin toxicity that was not a rash or was not related to EGFR inhibitor treatment, they included a description of symptoms only, they did not include enough details on treatment types or doses, timelines for observed responses, or specific outcomes, they were not accessible through the library system, or they were published prior to the year 2000. An additional four articles were identified by hand-searching the references of articles obtained through the electronic search.

Number of Source Documents

A total of 38 primary research studies and 11 published guidelines, recommendations, or consensus statements were identified for consideration in the final evidence review.

Methods Used to Assess the Quality and Strength of the Evidence

Not stated

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Evidence was selected and reviewed by a working group comprised of members from these three provincial Tumour Teams and a Knowledge Management (KM) Specialist from the Guideline Utilization Resource Unit (GURU). A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field).

Evidence Tables

Evidence tables containing the first author, year of publication, patient group/stage of disease, methodology, and main outcomes of interest are assembled using the studies identified in the literature search. Existing guidelines on the topic are assessed by the KM Specialist using portions of the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument (http://www.agreetrust.org) and those meeting the minimum requirements are included in the evidence document. Due to limited resources, GURU does not regularly employ the use of multiple reviewers to rank the level of evidence; rather, the methodology portion of the evidence table contains the pertinent information required for the reader to judge for himself the quality of the studies.

The table in Appendix B in the original guideline document contains a summary of English-language published guidelines and consensus statements for the management of mild, moderate, and severe rashes.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Formulating Recommendations

The working group members formulated the guideline recommendations based on the evidence synthesized by the Knowledge Management (KM) Specialist during the planning process, blended with expert clinical interpretation of the evidence. As detailed in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field), the working group members may decide to adopt the recommendations of another institution without any revisions, adapt the recommendations of another institution or institutions to better reflect local practices, or develop their own set of recommendations by adapting some, but not all, recommendations from different guidelines.

The degree to which a recommendation is based on expert opinion of the working group and/or the Provincial Tumour Team members is explicitly stated in the guideline recommendations. Similar to the American Society of Clinical Oncology (ASCO) methodology for formulating guideline recommendations, the Guideline Utilization Resource Unit (GURU) does not use formal rating schemes for describing the strength of the recommendations, but rather describes, in conventional and explicit language, the type and quality of the research and existing guidelines that were taken into consideration when formulating the recommendations.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This guideline was reviewed and endorsed by members of the Alberta Provincial Thoracic Malignancies, Gastrointestinal, Head and Neck, and Breast Tumour Teams.

When the draft guideline document has been completed, revised, and reviewed by the Knowledge Management (KM) Specialist and the working group members, it is sent to all members of the Provincial Tumour Team for review and comment. This step ensures that those intended to use the guideline have the opportunity to review the document and identify potential difficulties for implementation before the guideline is finalized. Depending on the size of the document, and the number of people it is sent to for review, a deadline of one to two weeks will usually be given to submit any feedback. Ideally, this review will occur prior to the annual Provincial Tumour Team meeting, and a discussion of the proposed edits will take place at the meeting. The working group members will then make final revisions to the document based on the received feedback, as appropriate. Once the guideline is finalized, it will be officially endorsed by the Provincial Tumour Team Lead and the Executive Director of Provincial Tumour Programs.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate prevention and treatment of rash in patients treated with epidermal growth factor receptor (EGFR) inhibitor therapies

Potential Harms

Not stated

Qualifying Statements

Qualifying Statements

The recommendations contained in this guideline are a consensus of the Alberta Provincial Thoracic Malignancies, Gastrointestinal, and Head and Neck Tumour Teams and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

Implementation of the Guideline

Description of Implementation Strategy

- Present the guideline at the relevant local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services Web site.
- Send an electronic notification of the new guideline to all members of CancerControl Alberta.

Implementation Tools

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 May

Guideline Developer(s)

CancerControl Alberta - State/Local Government Agency [Non-U.S.]

Source(s) of Funding

CancerControl Alberta

Guideline Committee

Alberta Provincial Thoracic Malignancies, Gastrointestinal, and Head and Neck Tumour Teams

Composition of Group That Authored the Guideline

Members of the Alberta Thoracic Malignancies, Gastrointestinal, Head and Neck, and Breast Tumour Teams include medical oncologists, radiation oncologists, surgeons, surgical oncologists, nurses, pathologists, pharmacists, and allied health care professionals.

Financial Disclosures/Conflicts of Interest

Participation of members of the Alberta Provincial Tumour Teams in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Tumour Teams are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the Alberta Health Services Web site .

Availability of Companion Documents

The following is available:

- Guideline utilization resource unit handbook. Edmonton (Alberta): CancerControl Alberta; 2013 Jan. 5 p. Electronic copies: Available from the Alberta Health Services Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on August 12, 2014. The information was verified by the guideline developer on September 25, 2014.

Copyright Statement

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